



Vitamin Studies: Rebuttal to allegation that certain vitamins may shorten lifespan

Reprinted with permission from Life Extension Foundation, USA

It is almost inconceivable to think that for the greater part of the 20th century, a “scientific” debate raged as to whether cigarette smoking was dangerous. An even longer running controversy focused on whether food choices (i.e. diet) had any effect on how long people lived. It was not until the later part of the 20th century that the FDA admitted that high saturated fat diets increase heart attack risk.

Today’s unanimous recommendation to eat lots of fresh fruits and vegetables is a relatively recent phenomenon. Back 50 years ago when mid-life heart attack rates were nearly triple what they are now, it was not unusual for people (especially men) to eat virtually no fruits or vegetables. Even now, the processed food industry heavily lobbies government agencies to not recommend disease-preventing foods to the public.

Just as companies that profited by selling cigarettes and processed foods egregiously misled the public in the past, today’s consumers are confronted with so-called “scientific” reports that question the value of some dietary supplements.

A report released on April 16, 2008 went as far as to suggest that certain vitamins might shorten lifespan. All of this is reminiscent of the scientific charade perpetrated by tobacco companies who falsely claimed that cigarettes did not cause lethal disease. In this case, the econom-

ic beneficiaries will be pharmaceutical companies who can expect increased sales of prescription drugs to those who fall for the latest media hype.

As the Life Extension Foundation has done for the past 28 years, we will succinctly separate the facts from the fiction so our members can draw a rationale conclusion about this latest hoax.

Outlandishly low and high potencies evaluated

As has been the case of previous studies conducted by mainstream doctors, the potencies of the nutrients evaluated in this negative report are far different than what knowledgeable health conscious consumers take on a daily basis.

This report condemning supplements claimed that vitamin A caused a 16% increased risk of dying. The vitamin A potencies given to study subjects ranged from 1,333 IU to 200,000 IU a day, or taken every other day, or in one case, ingested just once! Yes, a trial used to vilify this nutrient gave the participants one dose of vitamin A. When these nursing home subjects did not show greater survival benefits, the authors of this negative report blamed the single dose of vitamin A for the deaths.

We don’t know of anyone who actually takes their vitamin A in these kinds of doses, but these were the very studies used to assassinate vi-

tamin A.

This negative report also claimed a 4% increased risk of dying in those who took vitamin E. One might speculate that the failure to supplement with gamma tocopherol may have caused this mortality increase (we discuss more about this later).

The stark reality is that the potencies of alpha tocopherol vitamin E evaluated in the negative report ranged from 10 IU to 5000 IU, which of course has nothing to do with what informed consumers are actually taking. In fact, 10 IU of vitamin E does not even meet the daily minimum requirement for this nutrient. Nonetheless, the authors of this negative report included this study with a host of others to attack vitamin E.

For beta-carotene, the authors claimed a 7% increased risk of death. Doses evaluated ranged from 2000 IU to 83,350 IU. We don’t know of anyone taking this high dose of beta-carotene, but these studies were nonetheless used to further frighten the public against this supplement.

Study periods evaluated ranged from 28 days to 12 years. The authors apparently thought that study periods as short as 28-days were long enough to include in their attack against certain vitamins.

As you will read next, these details about potencies have little meaning when one learns of the study-selection bias that resulted in 91% of evaluable vitamin studies being



omitted from the analysis.

Most vitamin studies excluded from report

Out of a total of 815 vitamin studies considered for evaluation, 748 studies were excluded from the analysis (only 67 trials were included in the final report). Here are the absurd reasons given for excluding these 748 studies:

405 trials out of the 748 were removed from the statistical analysis plan because there were no deaths reported in any of the treatment arms. Therefore, this meta-analysis excluded 405 trials that showed no increase in mortality risk.

245 studies out of the 748 were removed from the statistical analysis plan because the authors' inclusion criteria were not fulfilled. Double-blind, randomized, controlled intervention studies were excluded in the analysis for a number of reasons that can only be described as so exacting that many studies published in the *New England Journal of Medicine*, *JAMA*, and other top-tier medical journals would fail these criteria. Here were reasons given for excluding these 248 studies:

- Specific allocation methods for study participants were not described in detail.
- A combination of dates and/ or 'admittance' numbers was used to randomize participants rather than complex study participant identifier codes.
- Methods used to hide the method of vitamin allocation were not described in detail.
- The specific method of blinding was not described in detail
- There were no drop-outs or withdrawals but the exact reason(s) for the lack of drop-outs or withdrawals were not described in detail
- In trials with participants that dropped out or withdrew, the exact number and/ or specific reason for drop-out or study withdrawal was not described in detail

So while the media was running headlines like "Taking Vitamins May

Shorten Your Life", the report the headline was based on omitted most of the vitamin studies that should have been included. This obvious bias rendered the findings meaningless, and we applaud certain news networks who withdrew this defective report from their websites within hours of posting it. One news network even followed with a positive report on the value of antioxidants.

Flawed statistical analysis

The authors used a variety of statistical tools and models to manipulate the data used in the negative report. One way they did this was to use both a 'random effect' model, and a 'fixed effect' model.

Much of what we are going to say here will be confusing to lay people. The reason we have to include it is that this entire report was based on statistical models chosen by the report's authors. As many of you know, when attempting to conduct a meta-analysis this extensive, statistical methods can be used to create conclusions that may differ considerably from what the underlying data reveal.

The 'random effect' model can be used to identify for difference of effect of antioxidant vitamins on separate patient populations (for example, to assess for the effect of vitamins on cancer patients as against heart disease patients). The 'random effect' model can also be used to help determine if different doses of an antioxidant vitamin have different effects (for example, whether a high dose of vitamin A is associated with mortality risk in contrast to a low dose of vitamin A).

For this meta-analysis, the 'random effect' model can be used to evaluate if different doses and/ or single or combined antioxidants and/ or interventions significantly affects mortality. Out of the 67 studies included in the meta-analysis, antioxidants were administered alone, or in combination with other interventions (e.g. drugs, minerals, other antioxidants) daily or on alter-

nate days for 28 days to 12 years at a very wide range of dosages, such as 10 IU to 5000 IU for vitamin E.

In this meta-analysis, the authors found that the 'random effect' model was not significant, meaning it failed to show an increase in mortality. So they used instead the 'fixed effect' model to show a 4% increased risk.

In essence, the results of this meta-analysis suggest that different doses of vitamins, different patient populations, and single vs. combined antioxidants had absolutely no effect upon mortality risk when the initial statistical model is used, but that vitamins increase mortality risk regardless of dose or patient population when a different statistical model is substituted. This is patently absurd, and calls into question the entire legitimacy of this meta-analysis.

In point of fact, the authors of this flawed meta-analysis were asked to only include the 'random effects' model in a prior presentation of this data in the *Journal of the American Medical Association (JAMA)* (Bjelakovic 2007a). By using the 'fixed effect' statistical model and excluding fully 91% of the eligible studies for the analysis, the authors succeeded in achieving headlines by selectively emphasizing models that achieved statistical significance.

Most of the analyzed studies were done on sick people

This negative report attacking certain supplements recommends that healthy people should not take these nutrients, yet 46 out of the 67 studies that were evaluated were conducted on subjects that were diagnosed with disease.

The studies cannot relate mortality differences based on these vitamins

More than 60% of Americans regularly ingest some sort of dietary supplement. The question is, are the 60% of Americans taking supplements



going to live longer than those who don't? An analysis of the scientific literature indicates they probably won't.

The reason is that few Americans are taking enough of the proper nutrients to duplicate the clinical studies showing that the diseases of aging may be preventable.* Twenty-eight years ago, the Life Extension Foundation began a systematic review of published scientific findings relating to the prevention of degenerative disease and aging. The results of this painstaking investigation provided convincing evidence that the killer diseases of aging could be largely prevented by the proper intake of nutrients, hormones, certain drugs, and lifestyle changes.*

The phenomenon known as aging is a result of a number of pathological changes that are somewhat controllable using existing technologies. By prolonging our healthy life span, we put ourselves in a position to take advantage of future medical breakthroughs that may result in dramatic extensions of the human life span. Here are some of the underlying controllable causes of the diseases of aging we know of today:

1. Chronic inflammation.

Aging people suffer an epidemic of outward inflammatory diseases such as arthritis, but chronic inflammation also damages brain cells, arterial walls, heart valves, and other structures in the body. Heart attack, stroke, heart valve failure, and Alzheimer's senility have been linked to the chronic inflammatory cascade so often seen in aging humans.*

2. Glycation.

It is well known that diabetics age prematurely, but even non-diabetics suffer from a devastating chemical reaction called glycation, where protein molecules bind to glucose molecules in the body to form non-functioning structures. Glycation is most evident in senile dementia, stiffening of the arterial system, and

degenerative diseases of the eye.*

3. Methylation Deficit.

Cellular DNA requires constant enzymatic actions (methylation) for maintenance and repair. Aging cripples youthful methylation metabolism causing DNA damage that can manifest as cancer, liver damage, and brain cell degeneration.*

4. Mitochondrial Energy Depletion.

The cell's energy powerhouse (the mitochondria) requires a complex series of chemicals to be present in order to maintain critical functions such as transporting nutrients through the cell membrane and purging the cell of toxic debris. Mitochondrial energy depletion can result in congestive heart failure, muscle weakness, fatigue, and neurological disease.*

5. Hormone Imbalance.

The trillions of cells in the human body are delicately synchronized to function by chemical signals called hormones. Aging creates a severe hormone imbalance that is often a contributing cause to many diseases associated with aging including depression, osteoporosis, coronary artery disease, and loss of libido.*

6. Excess Calcification.

Calcium ions are transported into and out of cells through calcium channels in the cell membrane. Aging disrupts calcium transport, and the result is excess calcium infiltration into cells of the brain, heart valves, and middle arterial wall (causing arteriosclerosis).*

7. Fatty Acid Imbalance.

The body requires essential fatty acids to maintain cell energy output. Aging causes alterations in enzymes required to convert dietary fats into the specific essential fatty acids the body requires to sustain life. The effects of a fatty acid imbalance may manifest as an irregular heart beat, joint degeneration, low energy, hy-

per-coagulation, dry skin, or a host of other common ailments associated with normal aging.*

8. DNA Mutation.

Numerous synthetic and natural compounds mutate cellular DNA and cause cancer cells to form. Aging cells lose their DNA gene repair mechanisms and the result is that DNA genetic damage can cause cells to proliferate out of control, i.e., turn into cancer cells.*

9. Immune Dysfunction.

For a variety of reasons, the aging immune system loses its ability to attack bacteria, viruses, and cancer cells. In aging humans, excessive levels of dangerous cytokines are produced that cause the immune system to turn on its host and create autoimmune diseases associated with aging such as rheumatoid syndrome.*

10. Non-Digestive Enzyme Imbalance.

Internal cellular functions depend on multiple enzymatic reactions occurring with precise timing. Aging causes enzyme imbalances primarily in the brain and liver, which results in severe neurological diseases such as Parkinson's or the persistent memory loss aging people so often complain about. Impaired liver function results in toxic damage to every cell in the body.*

11. Digestive Enzyme Deficit.

The aging pancreas often fails to secrete enough digestive enzymes, while the aging liver does not secrete enough bile acids. The result is chronic indigestion people complain about as they age.*

12. Excitotoxicity.

The aging brain loses control of its release of neurotransmitters such as glutamate, resulting in devastating brain cell damage and destruction.*

13. Circulatory Deficit.

Microcapillary perfusion of blood to



the brain, eye, and skin is impaired as a part of normal aging. The result is that disorders of the eye (such as cataract, macular degeneration, and glaucoma) are the number one aging-related degenerative disease. Major and mini-strokes are common problem associated with circulatory deficit to the brain. The skin of all aged people show the effects of lack of nutrient-rich blood to the upper layers.*

14. Oxidative stress.

Free radicals are unstable molecules that have been implicated in most diseases associated with aging. Antioxidants have become popular supplements to protect against free radical-induced cell damage, but few people take the proper combination of antioxidant supplements to adequately compensate for age-induced loss of endogenous antioxidants such as SOD and catalase.*

Notice that oxidative stress is listed as number 14 on the above list of controllable factors that cause aging-related diseases. While suppressing the free radicals that cause oxidative stress protects against many disorders, there is clearly much more that can be done to stave off aging than merely taking antioxidant supplements.* Children can benefit by taking vitamin supplements, but it is the aging human whose body is depleted of the endogenous antioxidants, hormones, enzymatic repair systems, and other biological chemicals needed to sustain life. What is optional in childhood turns out to be mandatory as humans enter middle age and become vulnerable to the plethora of degenerative diseases that await them if they do not adequately protect themselves.*

The Life Extension Foundation has designed a scientific program to counteract the known biochemical processes proposed (by gerontologists) as primary causes of aging. The TOP TEN Most Important Steps for Achieving Ultimate Health <<http://www.lef.org/Vitamins-Supplements/Top10/index.htm>>

provides recommendations to neutralize many of these known causes of premature aging.* Based on the 14 known mechanisms of aging, it is ludicrous to look at a group of mostly ill study subjects taking unusual doses of vitamin A, vitamin E or beta-carotene and then expect to see a significant benefit. There are too many other nutrients and hormones that even healthy aging people need to extend their healthy lifespan. Fortunately, most Life Extension members are taking these nutrients and hormones in the proper doses. Read more about the epidemic deficiency of vitamin E <http://www.lef.org/magazine/mag2007/mar2007_aws_i_01.htm> .

Conclusion

In today's Western world, a large percentage of the population fails to ingest optimal potencies of many essential nutrients. As you will read in part two of this report, a shocking majority (93-96%) of people of people who don't supplement with vitamin E are deficient in vitamin E.

This negative report attacking supplements is fatally flawed because it:

1. Omitted 91% of the studies that measured the effects of these vitamins on human subjects including all studies for which there was no mortality!
2. Included studies that used doses far below or far above what health conscious people actually supplement with.
3. Chose to bias the reporting of the results by emphasizing one type of statistical model that showed a significant effect rather than another statistical model that did not show a significant effect.
4. Failed to account for the 14 mechanisms involved in aging and premature death. For example, it is absurd to think that taking 1,333 IU to 200,000 IU of vitamin A is going to have meaningful impact when there are more than one hundred individual components to a science-based death reduction program.

The final shocker is that this meta-analysis report attacking vitamin A, beta-carotene and vitamin E is not new. It was in fact published last year and drew a lot of criticism for the obvious flaws it contains. Perhaps the reason this story was quickly removed from media websites on the day it appeared is that the broadcasters realized they were not relaying "news", but instead regurgitating anti-supplement propaganda.

Needless to say, even this brief exposure was a public relations score for pharmaceutical interests, as millions of people worldwide may be frightened away from supplements that could reduce their future need for expensive prescription drugs.